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Original Research Article

Comparing the efficacy of 7%, 5% hypertonic saline and 0.9% normal saline in acute bronchiolitis: a randomized controlled trial

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ABSTRACT

Background: The study aimed to investigate the effect of nebulized 5% and 7% Hypertonic Saline (HS) versus Normal Saline (NS) in acute viral bronchiolitis.
Methods: This is a prospective, randomized controlled trial study that has been done on 90 infants presenting with acute bronchiolitis. All infants divided randomly in three equal size and matched groups (n=30). Subjects received 4ml nebulized 5% and 7% HS along with 0.15mg/kg Adrenaline or 4 ml 0.9%NS every 6 hours from enrolment until hospital discharge. For all patients, clinical symptoms such as sputum, wheezing, retraction rate, heart rate, fever, crackle, irritability, week nutrition and breathing were recorded in baseline and length of wheezing, cough, and crackle, length of stay (LOS), fever and sputum based on days in the end of study. Collected data analyzed by statistical methods in SPSS.19.
Results: At baseline, study groups were similar in demographic and clinical characteristics. The mean age of all patients was 5.5±3.6 months, and 59 (65.6%) were male. The length of cough and crackle, and the length of LOS in 5% and 7% HS groups was significantly lower than NS group.
Conclusions: Among infants admitted to the hospital with viral bronchiolitis, treatment with nebulized 5% HS and 7% HS had significant effect on decreasing clinical symptoms length and LOS when compared with NS.

Keywords: Acute bronchiolitis, Hypertonic saline, Infants

INTRODUCTION

Acute viral bronchiolitis is one of the most common causes of lower respiratory tract infection during infancy and also the most common cause of hospital admission among infants and young children in many countries. Bronchiolitis is most common in the first 2 years of life.[1,2]

Usually, the child first experiences colds, such as cough, runny nose, and after two or three days, a sudden onset of breathing, wheezing, swollen and superficial breathing (up to 60 times per minute), interstitial spaces and abdomen (Swirling movements), coughing, fever, wheeze and crackle in the lungs, nasal sprains, the use of subcutaneous muscles and increased heart rate, decreased oxygen saturation.[3]

For disease diagnosis, laboratory and radiologic check is not usually needed. Diagnosis of bronchiolitis is a clinical diagnosis and is done based on patient history, physical examination and exclusion of other causes of respiratory distress. For bronchiolitis no short-term or long-term treatment has ever been confirmed and the treatment is still supportive and oxygen prescription, fluid and suction secretions from the upper airway and mechanical ventilation if necessary. In cases where the pathogen is a

virus, antibiotic treatment is not necessary and only the symptoms such as fever and wheezing are treated.[4-7]

Currently the inhalation of HS as a treatment option has been proposed and the conducted limited studies in this area have shown that the use of HS has been useful in improving severity scores and the reduction of LOS.[7-13] Adrenaline inhalation as a common routine treatment used for bronchiolitis, in addition to expanding the bronchi, may reduce mucosal edema. Considering the limited number of studies and the lack of similar trials in this country Iran, this study was aimed to investigate the effect of nebulized 5% and 7% Hypertonic Saline (HS) versus Normal Saline (NS) in acute viral bronchiolitis.

METHODS

Authors conducted a prospective, randomized controlled trial in 90 infants presenting with acute bronchiolitis.

Patient selection

Informed consent was obtained from a parent or legal guardian of each infant enrolled in the study. Patients age 8 weeks to ≤24 months admitted to the children hospital between April 2016 to Sep 2016 with bronchiolitis (defined as first episode of respiratory distress with wheezing and viral) and a bronchiolitis severity score (BSS) more than 4 were eligible for the study (Table 1).[14]

Table 1: Assessment of bronchiolitis severity in infants based on RDAI scale.

Score symptoms		0	1	2	3
Wheezing	While exhaling	None	Exhale end	Half an Exhale	Three quarters of an exhale
	While respire	None	Incomplete	Complete	-
	Number of lobes involved in the lung	0	1 or 2	3 or 4	-
Retraction	Supraclavicular	None	Mild	Moderate	Severe
	Between the ribs	None	Mild	Moderate	Severe
	below the rib cage	None	Mild	Moderate	Severe

Inclusion criteria included age ≤24 months, diagnosis of bronchiolitis by pediatrician by clinical examination of wheezing and viral detection and CXR. We excluded infants who had pulmonary and heart disease, Down syndrome, immune deficiency, metabolic disease, inhaled brunch dilator uses or previous episodes of wheezing.

Study protocol

All eligible patients were randomized to 1 of 3 groups. The study groups received 0.15 mg/kg Adrenaline with 4 ml nebulized 5% and 7% HS, respectively and the control group received 0.15 mg/kg Adrenaline with 4 ml 0.9% NS every 6 hours from enrolment until hospital discharge.

LOS and recovery time of clinical symptoms such as cough, wheezing and sputum and other symptoms for all groups were recorded in following days (end of study) objectively by clinical examination by pediatrician. Also, infants were systematically monitored for adverse events during the hospitalization and followed with a phone call by research personnel two weeks after hospital discharge.

Statistical analysis

Authors compared patient demographic and clinical characteristics between groups by using chi-square test for categorical variables and t-test and ANOVA for compare the means between two and three groups. The significant level was set as $p<0.05$.

This study was approved in ethics committee of Ardabil University of medical sciences with number of arums.rec.1394.19 and registered in Iran clinical trials web pages with code IRCT2015090717843N5.

RESULTS

The mean age of the total patients was 5.5 ±3.6 months and most of them were in the age group of 2 to 6 month (58.9%). Of all patients, 59 (65.6%) were male and 19 (2.1%) had taken antibiotics before admission to study. All three groups are similar in-Patient characteristics and clinical symptoms in the admission to study (Tables 2 and Table 3).

Table 2: Characterized of patients in the start of study before intervention.

Groups Variables	0.9% Normal saline, n=30	5% HS, n=30	7% HS, n=30	p-value
Age, mo, mean±SD	5.7±4.8	5.5±3	5.2±2.6	0.88
Gender, male	20/30 (33.9%)	22/30 (37.3%)	17/30 (28.8%)	0.39
Duration of symptoms, mean±SD	2.13±1	1.7±0.7	1.8±0.7	0.096
Antibiotic use	9/30 (47.4%)	6/30 (31.6%)	4/30 (21.1%)	0.28

Table 3: Frequency of clinical symptoms in patients in baseline by three groups.

Symptoms	0.9% Normal Saline, n=30	5% HS, n=30	7% HS, n=30	p-value
Sputum	5 /30 (16.7%)	7/30 (23.3%)	4/30 (13.3%)	0.58
Wheezing	30 /30 (100%)	30/30 (100%)	30/30 (100%)	1
Crackle	25/30 (83.3%)	27/30 (90%)	27/30 (90%)	0.78
Retraction	9/30 (30%)	15/30 (50%)	13/30 (43.3%)	0.28
Increased breathing	23/30 (76.7%)	24/30 (80%)	27/30 (90%)	0.37
Fever	11/30 (36.7%)	17/30 (56.7%)	12/30 (40%)	0.25
Irritability	4/30 (13.3%)	5/30 (16.7%)	5/30 (16.7%)	1
Week nutrition	21/30 (70%)	14/30 (46.7%)	16/30 (53.3%)	0.17
Increased hearth rate	3/30 (10%)	4/30 (13.3%)	6/30 (20%)	0.65

There was significant difference in the mean length of cough, Crackle and LOS between three groups. But there wasn't significant difference between three groups in terms of Wheezing, fever, and sputum (Table 4).

Table 4: Compare the clinical symptoms in three groups in the end of study.

Symptoms	0.9% Normal Saline, n=30	5% HS, n=30	7% HS, n=30	p-value
Length of wheezing (day)	3.4±1.1	3.03±1.13	2.97±0.9	0.23
Duration of cough (day)	3.1±1.4	2.3±1.6	2.33±1.12	0.044
Length of Crackle(day)	1.63±1.2	0.87±0.9	0.8±1	0.003
Length of stay (LOS) (day)	4.13±1.1	3.37±1.1	3.23±0.9	0.002
Length of fever (day)	0.33±0.5	0.5±0.51	0.4±0.49	0.427
Length of sputum (day)	0.4±1	0.1±0.4	0.23±0.8	0.307

The mean of LOS in two interventional groups within age groups of 2 to 6 months (P=0.003) and 6 to 12 months (P=0.004) was significantly lower than control group.

In the age group 2 to 6 months, the mean length of crackle in patients receiving hypertonic saline 5% and 7% was significantly lower than control group. But another symptoms such as length of wheezing, cough, fever, sputum, need for oxygen therapy in two age groups 2 to 6 months and 6-12 months was similar between three groups.

DISCUSSION

In this study we showed that infants receiving 7% HS (P=0.004) and 5% HS (P=0.016) considerably recovered and discharged in a shorter period of time compared to infants receiving NS, but among two nebulized 7% HS and 5% HS there was no difference in this regard.

Most of previous studies showed that 3% HS is better than NS in the treatment of viral bronchiolitis in children which was in line with our study results but some studies showed it is not better than 0.9% NS.[8-19]

Many studies showed that 5% HS in treatment of bronchiolitis in children is better than 0.9% NS.[8,20,21]

Jacobs et al, conducted a clinical trial and showed that use of 7% HS with epinephrine did not have a considerable effect on the severity and LOS of the infants under 18 months with viral bronchiolitis which not in line with our study results.[22] All children in this study well tolerated the treatment and it was predictable because previous studies had shown that 7% and 5% HS are well tolerated by patients.[23,24]

Also in a study conducted by Goss and Ratjn, it was shown that 7% HS use in the treatment of cystic fibrosis in children under 6 years old is perfectly safe.[22] Regarding the safety of 5% HS, the study of Tinsa et al, showed that using it even without bronchodilator in infants under 12 months is well tolerated and had no significant complication.[20]

Like many similar studies, in this study, along with 7% HS, 5% HS, and NS, 0.15mg/kg adrenaline was used in all three groups.[8,10,19,20,24-28] Hypertonic saline was shown to be more effective than NS in improving bronchiolitis clinical scores in 5 studies in both outpatient and inpatient settings.[29-33]

Five studies noted that LOS for patients who received hypertonic saline was shorter than for those given NS, which is consistent with the results of our study.[11,12,31-33]

One of the findings of the present study was the considerable reduction in LOS in both two 7% HS and 5% HS receiving groups compared to NS control group which in addition to its clinical importance, can cause a significant reduction in the cost of patients treatments. In line with the findings of our study, in the studies of Zamani et al, and Mandlberg et al, recovery duration of 3% HS group was significantly lower than patients with NS.[9,16] On

the contrary, the study of Tinsa et al, did not show any significant difference in LOS between two groups of 5% HS and NS.[20] In the study of Jacobs et al, there was no difference in LOS of infants with bronchiolitis receiving 7% HS with NS.[24] Our study did not reveal a difference between 7% and 5% HS in terms of cough length, crackles length or LOS but in compared with NS the difference was significant.

CONCLUSION

This study showed that using 5% and 7% HS in compare with NS have significant effect on the Reducing the recovery time, discharge from the hospital and also duration of coughing and crackle in 2-24 month infants with viral bronchiolitis. Also authors found that using each of 5% HS or 7% HS was similar affect in treatment of viral bronchiolitis and hadn't any significant side-effects in infants and well tolerated by them. Authors recommended that doing multi-center studies with bigger sample size and more systematic review studies for better response to arisen contradictions of this study with other studies in future is necessary.

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